

# Capturing the Cacophony of Movement

Citation for published version (APA):

Mentzel, T. (2018). *Capturing the Cacophony of Movement: Assessment, epidemiology and treatment of movement disorders in patients with psychotic disorders*. [Doctoral Thesis, Maastricht University]. Datawyse / Universitaire Pers Maastricht. <https://doi.org/10.26481/dis.201800607tm>

**Document status and date:**

Published: 01/01/2018

**DOI:**

[10.26481/dis.201800607tm](https://doi.org/10.26481/dis.201800607tm)

**Document Version:**

Publisher's PDF, also known as Version of record

**Please check the document version of this publication:**

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

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## Valorisation



The primary rationale behind this thesis is to improve the lives of patients with severe mental illness (SMI) suffering from movement disorders. The following pages offer a critical review of the practical, economic, and social values of this thesis. This review is split into two sections. The first section covers what we have learned about prevalence, incidence, and persistence of movement disorders and the treatment of tardive dyskinesia. In the second section, the potential of assessing movement disorders instrumentally is discussed.

## **Prevalence of movement disorders in second-generation antipsychotics**

In the Netherlands, SMI affect the lives of roughly 280,000 individuals[1]. Quality of life is hindered in patients with SMI and movement disorders are a predictor for deterioration of quality of life. Movement disorders can be socially stigmatizing, socially impairing, and lead to employment difficulties and isolation[2-4]. The socio-economic cost of SMI is expected to be high, as ongoing psychiatric care is often needed for the symptoms and side effects of SMI and SMI often lead to prolonged leave of absence from work or unemployment. It is concerning that movement disorders can motivate treatment non-adherence in patients[5], because this can result in relapse and psychotic episodes which substantially increases the cost of treatment. Our analysis of the GROUP study[6] made apparent that movement disorders are prevalent in roughly 40% of the patients of this cohort and persisted in more than 50% of the cases. The high prevalence and socio-economic burden of movement disorders stress the importance of investigating means of preventing and treating movement disorders in patients with SMI.

## **Switch to clozapine in patients with tardive dyskinesia**

The results of the GROUP study show that movement disorders are still prevalent despite treatment with SGAs being predominant. In search of possible treatment strategies for tardive dyskinesia, we performed a meta-analysis to investigate the effect of switching to clozapine on tardive dyskinesia. Overall the effect of a switch to clozapine on tardive dyskinesia was a significant reduction in severity. Especially promising was that in patients with moderate to severe forms of tardive dyskinesia the reduction of tardive dyskinesia was substantial. The advice to switch to clozapine in patients with moderate to severe forms of tardive dyskinesia can be implemented in clinical guidelines and in clinical routines. This offers a tremendous relief for patients, as severe cases of orofacial tardive dyskinesia can impair speech, chewing and swallowing, can motivate medication non-adherence, and it is stigmatizing and often contributes to social isolation.

## Instrumental measurement of movement disorders

The negative impact of movement disorders on patients' social and physical wellbeing and their high prevalence warrant regular screening in order to manage their symptoms as best as possible. We developed two instruments that aid in the simple and reliable screening of movement disorders. The feasibility and validity of assessing bradykinesia were demonstrated experimentally. With this instrument, it is much easier to assess movement disorders than the current solution where a trained psychiatrist performs the assessment to obtain reliable results. This instrument can save time and money seeing that this screening can now be offloaded to other clinical staff members. Moreover, preventing movement disorders from burdening patients can prevent a relapse in their SMI, as it can help prevent medication non-adherence. A logical next step would be to explore the potential market and determine whether instrumentally assessing movement disorders is commercially viable. Questions that remain to be answered are; what the possible economic savings can be for mental hospitals, private clinics and health insurance companies. What the expected costs would be for developing a commercial product taking into account such things as the cost of the development, production, regulatory approval, marketing and support.

Another potential application for the instrumental assessments is screening for subtle signs of the dysregulation of motor control that cannot be detected via conventional clinical techniques. For example, by using proven technologies to assess force variability[7-10] or by using smartphones and wearables to continuously monitor for signs of movement disorders[11, 12]. Subtle motor signs can help differentiate among psychotic disorders[13] and could potentially even identify individuals at risk of developing psychosis[10, 14, 15]. Further research is still necessary to determine whether these motor signs actually are a biomarker for psychosis. Moreover, it also remains unclear whether early interventions are warranted as their effect is still being studied[16]. The portable and affordable instrument we developed to detect force variability is very useful for these studies and enables them to study force variability sensitively in large numbers of patients. If the results of these biomarker/prediction studies are positive this could have tremendous implications. Preventing psychosis and better management of its symptoms can substantially improve the quality of life of many patients, not to forget the lives of their friends and relatives, and considering the long length of treatment it can save a vast amount of money on healthcare.

Altogether, our work on capturing subtle motor abnormalities and movement disorders instrumentally is a step towards the implementation of these techniques in routine clinical care. The potential for the commercialization of these techniques is growing. We see a future in which these instruments will improve the quality of life of many patients and perhaps in some cases even help prevent the onset of psychosis.

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